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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,252	07/25/2005	Shunichi Kuroda	12480-000069/US	1324

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EXAMINER	
HORNING, MICHELLE S	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,252	KURODA ET AL.	
	Examiner	Art Unit	
	Michelle Horning	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *7 and 14-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 8-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office action is responsive to communication filed 10/09/2007. The status of the claims is as follows: claims 1-6 and 8-13 are under current examination while claims 7 and 14-18 are withdrawn for being directed to non-elected inventions. Please note that this application has been forwarded to another Examiner and all correspondences regarding this application should be directed to Examiner Michelle Horning of AU 1648.

Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on 10/9/2007 is acknowledged.

Information Disclosure Statement

With the exception of an undated reference (see IDS filed 12/28/2004), the information disclosure statement submitted on 12/28/2004 and 9/28/2004 has been considered by the Examiner.

Drawings

Figures 1-8 filed 9/28/2004 have been accepted in its entirety by the Examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 and 8-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *at best* HBsAg-HSV1 tk particles (as defined by Figure 3) and size reduction in human hepatic cancer-derived tumors transplanted into rats, does not reasonably provide enablement for any and all nanoparticles as well as "a drug" for the "treatment" of any and all hepatic diseases in humans as so broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Enablement is considered in view of the *Wands* factors.

Nature of the invention. The claims are directed to a drug comprising hollow nanoparticles of a particle forming protein; these nanoparticles recognize a hepatocyte and further encapsulate a substance to be transferred to a cell for *treatment* of a hepatic disease. Further, the drug is administered to a human body via intravenous injection.

The state of the prior art. The instant specification discloses the following with respect to the prior art: "In a recently developed technique, a therapeutic gene is inserted in viral DNA, and the gene is transferred by an infectious virus. The method is innovative in the sense that it does not expose the site of transfer, is applicable to individuals, and provides nearly 100% uptake. However, the method suffers from a serious drawback in that the virus non-specifically infects a wide range of cells, transferring the gene to cells other than the target cell. Further, the method has a potential risk of unexpected side effect if the viral genome is incorporated in the

chromosomes. In fact, the method is not used in initial stages of disease treatment. Only the terminal patients can receive the benefit of the method" (paragraph 7).

The above submission, however, does not describe the *closest* prior art to the claimed inventions. Valenzuela et al (1985) describe a hybrid hepatitis B surface antigen/herpes simple 1gD particle and the underlying techniques for its production (see whole document). The authors teach that the hybrid particles successfully assemble into particles and that insertion of a foreign gene does not affect the particle assembly process (see page 325). The authors conclude that they have developed a new concept of hybrid HBsAg particles that improves epitope presentation of foreign antigens (also see page 325). Secondly, the teachings of WO 2000/46376 provide particles for gene therapy, comprising a protein envelope with a fusion protein, which comprises a virus protein, a cell permeability-mediating peptide and a nucleic acid present in the protein envelope (see Abstract). For convenience, any references made from this document will refer to its English-translated version, US Patent 7018826.

Scope of the claims. The claims are extremely broad in scope in that they encompass any and all nanoparticles, hepatitis B surface-antigen proteins and genes for the treatment of any and all hepatic diseases. It is further noted there is no structural limitations of the drug that correspond to the claimed function of treatment.

Guidance in the specification. The specification fails to provide any guidance of how the claimed drug successfully treats any and all hepatic diseases. In essence, the specification provides no guidance in how to use the claimed drug to achieve the successful effects as claimed. The figures merely disclose schematic drawings and a

graph depicting a reduction in size of a transplanted tumor following administration of a single drug. It is interesting and thus noted that Figure 3 depicts two different treatments of WiDr or NUE transplant animals without a control experiment in which no drug is administered to the transplant animals. WiDr is derived from human colon cancer-derived tumor tissue while NUE is derived from human hepatic cancer-derived tumor cells. It is not clear from the disclosure whether the dichotomy of results is due to effective treatment or the differential transplants involved. Applicant is invited to respond to this specific concern.

Working examples. With exception of the underlying nebulous experiment depicted in Figure 3, there are none. Also, note that there are no examples in which any drug is administered to a human body

Predictability in the art. There is no way the ordinary artisan could predict the structural requirements which would successfully achieve the treatment as so broadly claimed, especially according to the disclosure.

Amount of experimentation necessary. Much experimentation would still be required at multiple levels to both make and use the product as claimed. First, no structural requirements are defined and they could comprise anything leading to hollow nanoparticles encapsulating any substance. Secondly, the artisan would have to ascertain which combinations of nanoparticles and substance would work in leading to the "treatment of a hepatic disease". Thus, much undue experimentation is needed in determining both the crucial structure of the drug as well as the correlation of structure to function, if even possible.

Given the reasons above, it would require much undue experimentation for one of ordinary skill in the art to practice the full scope at the time the invention was made.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/46376. As noted above, its English translated version, US Patent 7018826 (hereinafter as "Hildt"), will be referred to for convenience.

Hildt discloses an invention relating to "nucleic acid containing particles which specifically bind to cells and can introduce their nucleic acid into these cells" (see paragraph 3). Additionally, Hildt describes a gene transfer system which is specific for a desired cell. In the case of liver cells, modified HBV vectors may be used, given its specificity for liver cells (see paragraph 4). Thus, the limitations of claims 1-3 and 8 have been met. Paragraph 17 describes genes which code for polypeptides and specifically provides tumor-associated antigens, meeting the limitation "cancer-treating gene" in claim 4. All of the limitations of the claims above have been met and these claims are rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hidlt and Xiang-Ling et al (2001). Claims 1-4 and 8 are rejected as discussed above. The Hidlt reference, however, fails to specifically teach or suggest thymidine kinase or HSV1tk.

Xiang-Ling et al disclose the killing effects of ganciclovir (GCV) on cells transduced with the HSV1-TK gene both *in vitro* and *in vivo* (see title). Cells transfected with the HSV1-TK gene are sensitive to GCV, a nontoxic antiviral drug (see Introduction). The authors demonstrate that the sensitivity of cells transfected with TK gene to GCV was 46 times higher than that of the parental cell (see Abstract). Further,

the authors note that "much literature previously reported that the sensitivity of transfected cells to GCV was enhanced 10^2-10^3 times than that of parental cells" (see page 904). It would have been obvious to one of ordinary skill in the art to combine the teachings of Hidlt and Xiang-Ling et al in order to make a particle specifically containing the HSV-TK gene. One would have been motivated to do so in order to target a specific cell (e.g. liver cell by HBV), introduce the HSV-TK gene and administer GCV in order to kill specific cells. There would have been a reasonable expectation of success, given the teachings of Xiang-Ling et al demonstrate the sensitivity of cells transfected with TK gene to GCV was 46 times higher than that of the parental cell (see Abstract). The invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5 and 8 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 2 of copending Application No. 10/509247 (PG Pub 20050181064). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to nearly identical products. More specifically, they are drawn to a hollow nanoparticle with the ability to recognize a hepatocyte and it encapsulates a substance.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-6 and 8-13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 4, 6, 8-12 of copending Application No. 10/509248 (PG Pub 20060165726). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to nearly identical products. More specifically, they are drawn to a hollow nanoparticle with the ability to recognize a hepatocyte and it encapsulates a substance. Further, the drugs are intravenously administered to humans.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-6 and 8-13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 8 and 14-16 of copending Application No. 10/509249 (PG Pub 20060088536). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to nearly identical products. More specifically, they are drawn to a hollow nanoparticle with the ability to recognize a hepatocyte and it encapsulates a substance. Further, the drugs are intravenously administered to humans.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-3 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4 and 9 of copending Application No. 10/529749 (PG Pub 20060292118). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to nearly identical products. More specifically, they are drawn to a hollow nanoparticle with the ability to recognize a hepatocyte and it encapsulates a substance.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michelle Horning whose telephone number is 571-272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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